

REMARKS

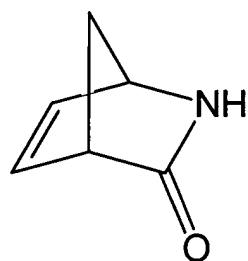
Reconsideration of this application is requested. Claims 2, 16, and 17 have been canceled without prejudice. Claim 1 has been amended to incorporate the limitations of claims 2 and 16, i.e., to recite that the heptenone (also known as the Vince lactam) is reduced with lithium borohydride. Claims 3-5 have been amended to depend from claim 1 rather than claim 1 or 2. Claims 21 and 22 have been amended to clarify that the heptenone is a (1R,4S)-2-azabicyclo[2.2.1]hept-5-en-3-one and (1S,4R)-2-azabicyclo[2.2.1]hept-5-en-3-one, respectively. The scope of claims 21 and 22 have not been narrowed by this amendment. Claim 24 has been added. Claims 1, 3-5, 18-22 and 24 are pending and at issue.

Claims 1-5 have been rejected as anticipated by Katagiri et al. and Taylor et al.

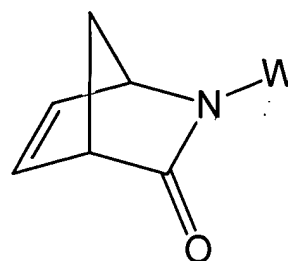
In the January 18, 2002 Office Action, the Examiner asserts that the same reactants are used in the presently claimed process as in the process disclosed by Katagiri and Taylor.

The presently claimed process (1) requires fewer reactants than that disclosed in Katagiri and Taylor and (2) obtains the aminoalcohol product by reacting the reactants in a different order.

In both Katagiri and Taylor, the Vince lactam is first substituted with an electron withdrawing group as shown below:



Vince Lactam



Substituted Vince Lactam

See, for example, chart 6 on page 1114 of Katagiri (an electron withdrawing group W is attached to compound 1 to yield compound 10c); and step i of scheme 3 on page 1123 of Taylor (a CO₂tBu group is attached to compound 1b (the Vince lactam) to form a substituted Vince lactam).

The substituted Vince lactam is then reacted with sodium borohydride to form the aminoalcohol. See, for example, lines 1-4 on the right column of page 1114 of Katagiri (compound 10c (the substituted Vince lactam) is reacted with sodium borohydride); and steps ii and iii on page 1123 of Taylor (the CO₂tBu substituted Vince lactam is reacted with sodium borohydride (NaBH₄) to form the aminoalcohol).

In the presently claimed process, the Vince lactam is not first substituted with an electron withdrawing group. Rather, the Vince lactam is directly reacted with a metal hydride, such as lithium borohydride.

Neither Katagiri nor Taylor disclose or suggest reacting the unsubstituted Vince lactam with a metal hydride, such as lithium borohydride, as recited in the pending claims.

Therefore, claims 1-5 are novel over Katagiri and Taylor and this rejection should be withdrawn.

Applicant does
intermediate
too,
see
pg. 5
of
spec.
Further,
claims
do not
exclude
intermediate
step

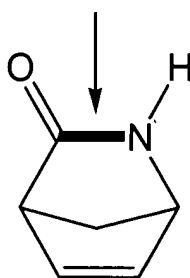
Claims 1-5 and 16-22 have been rejected under 35 U.S.C. §103(a) as obvious over Katagiri or Taylor in view of Wieczorek. Wieczorek allegedly teaches that lithium borohydride and sodium cyanoborohydride can be used as reducing agents in the preparation of aminoalcohols.

As discussed above, neither Katagiri nor Taylor disclose or suggest reacting the unsubstituted Vince lactam with a metal hydride, such as lithium borohydride, as recited in the pending claims.

Katagiri, Taylor, and Wieczorek do not provide any motivation or a reasonable expectation of success for reacting the Vince lactam with a metal hydride, such as lithium borohydride, to form the aminoalcohol recited in pending claim 1.

In fact, Katagiri found that it was necessary to add an electron withdrawing group W to the Vince lactam (2-azabicyclo[2.2.1]hept-5-en-3-one) in order to yield an aminoalcohol. See the last paragraph in the left column on page 1113. The aminoalcohol in Katagiri is formed by cleaving the amide bond in the Vince lactam:

The Amide Bond



Katagiri found "that if an appropriate electron-withdrawing substituent was introduced at the amide nitrogen ... the desired reductive C-N bond cleavage reaction proceeded smoothly" (left column, lines 35-38, page 1113). Katagiri also found that the aminoalcohol could not be

formed from the Vince lactam without first attaching a substituent to the nitrogen atom in the Vince lactam. See lines 1-4 on the right column of page 1114 of Katagiri.

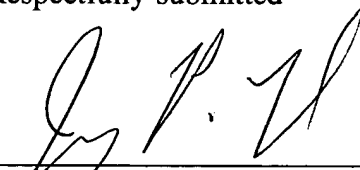
Based on the foregoing, one of ordinary skill in the art would not have a reasonable expectation based on Katagiri that the unsubstituted Vince lactam could be reduced with a metal hydride, such as lithium borohydride, to form an amino alcohol. Nor would one of ordinary skill in the art have the motivation to react the unsubstituted Vince lactam with a metal hydride, such as lithium borohydride, to form an aminoalcohol.

Therefore, this rejection should be withdrawn.

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted

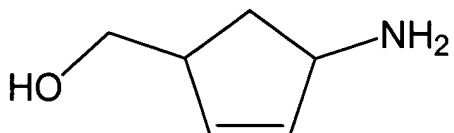


Jay P. Lessler
Reg. No. 41,151
Attorney for Applicants

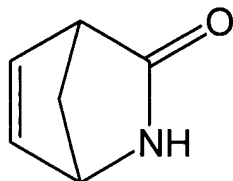
DARBY & DARBY
Post Office Box 5257
New York, NY 10150-5257
Phone (212) 527-7700

Marked-Up Claims
Accompanying July 17, 2002 Amendment
For U.S. Serial No. 09/198,427
(Docket No. 5409/OJ061)

1. (Twice Amended) A process for the preparation of an aminoalcohol of the formula



comprising the step of reducing 2-azabicyclo[2.2.1]hept-5-en-3-one of the formula



with [a metal hydride] lithium borohydride to form the aminoalcohol.

3. (Twice Amended) The process according to Claim 1 [or 2], characterized in that the reducing step is carried out at a temperature of from -20 to 200° C.

4. (Thrice Amended) The process according to Claim 1 [or 2], characterized in that the reducing step is carried out in a solvent selected from the group consisting of an aprotic organic solvent, protic organic solvent, and mixtures thereof.

5. (Thrice Amended) The process according to Claim 1 [or 2], characterized in that the reducing step is carried out in the presence of an additive selected from the group consisting of water and univalent and polyvalent C₁₋₆ alcohols.

18. (Unchanged) The process of claim 3, wherein the reducing step is carried out at a temperature of from 60 to 150° C.

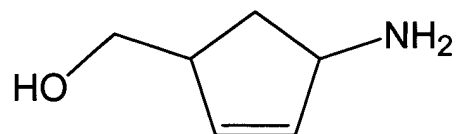
19. (Unchanged) The process of claim 1, wherein the 2-azabicyclo[2.2.1]hept-5-en-3-one is (1R,4S)-2-azabicyclo[2.2.1]hept-5-en-3-one, (1S,4R)-2-azabicyclo[2.2.1]hept-5-en-3-one, or a mixture thereof and the aminoalcohol is (1R,4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene, (1S,4R)-1-amino-4-(hydroxymethyl)-2-cyclopentene, or a mixture thereof.

20. (Unchanged) The process of claim 19, wherein the 2-azabicyclo[2.2.1]hept-5-en-3-one is a racemic mixture and the aminoalcohol is a racemic mixture.

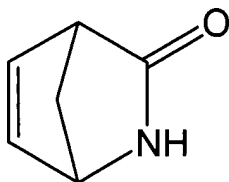
21. (Amended) The process of claim 19, wherein the 2-azabicyclo[2.2.1]hept-5-en-3-one is (1R,4S)-2-azabicyclo[2.2.1]hept-5-en-3-one and the aminoalcohol formed is (1R,4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene.

22. (Amended) The process of claim 19, wherein the 2-azabicyclo[2.2.1]hept-5-en-3-one is (1S,4R)-2-azabicyclo[2.2.1]hept-5-en-3-one and the aminoalcohol formed is (1S,4R)-1-amino-4-(hydroxymethyl)-2-cyclopentene.

24. A process for the preparation of an aminoalcohol of the formula



comprising the step of reacting 2-azabicyclo[2.2.1]hept-5-en-3-one of the formula



with lithium borohydride to form the aminoalcohol.